#### REMARKS

Claims 1, 8, 14, 55, 82, 84-85 and 87-88 have been amended. Additionally, Claims 7, 50-54 and 56-59 have been canceled. New Claims 89-99 have been added. The amendments to Claims 84 and 87-88, and new Claims 91-92, 96 and 98-99 are supported by the specification as originally filed, including, page 11, lines 8-14 and page 11, line 20 to page 12, line 4. Likewise, the amendments to Claims 82, 85-86 and 89, and new Claims 90, 93-95 and 97 are also supported by the specification as filed. For example, support for the amendments to Claims 82, 85-86 and 89, and new Claims 90, 93-95 and 97 can be found on page 5, lines 1-23 and page 12, line 8 to page 13, line 4. Claim 55 has been amended to include compounds exemplified in Examples 11, 12, 41, 49, 69, 71 and 77. Claims 7, 53-54 and 56-59 have been canceled merely to avoid any issues of double patenting with respect to U.S. Patent No. 6,815,458. In response to the Office Action mailed January 25, 2008, Applicants have carefully considered all of the rejections raised by the Examiner and respond thereto in detail below.

#### Rejection of Claims 1-14, 53-60 and 79-88 under 35 U.S.C. § 112, Second Paragraph

"substituted"

Claims 1-14, 53-60 and 79-88 stand rejected under 35 U.S.C. § 112, second paragraph because the patent office alleges that the term "substituted" is indefinite. As stated in the present specification, only aryl, heteroaryl, aralkyl and heteroaralkyl groups can be substituted. Furthermore, the possible substituents that can be present on the aforementioned groups is recited in the specification at page 11, lines 8-19 and page 11, line 20 to page 12, line 4. Thus, the term "substituted" as used in independent Claims 1, 8 and 14 is definite. Claims 2-7, 9-13, 53-60 and 79-88 depend directly or through another claims(s) to one of Claims 1, 8 and 14. Thus, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of Claims 1-14, 53-60 and 79-88.

#### "organyl group"

Claims 1-5 stand rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Applicants note that in the Response to the Restriction Requirement filed on December 21, 2007, "a cyclic or straight chained or branched acyclic organyl group" was

amended to recite "a straight-chained or branched alkyıl, a straight-chained or branched alkenyl, a straight-chained or branched alkenyl, a cycloalkyl, a cycloalkyl( $C_{1.6}$  alkyl)." This amendment is supported by the specification as originally filed, for example, on page 9, lines 20-34 and page 10, lines 1-6. Applicants respectfully submit that the terms "alkyl", "alkenyl", "alkynyl", "cycloalkyl" and "cycloalkyl( $C_{1.6}$  alkyl)" are terms well understood by those skilled in the art. In view of the amendment and the knowledge of those skilled in the art, Applicants respectfully submit Claim 1 is definite. Claims 2-5 depend directly or through another claim(s) to Claim 1. Therefore, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of Claims 1-5.

### Rejection of Claims 1-14, 53-60 and 79-88 under 35 U.S.C. § 112, First Paragraph "R"

As stated in the Office Action, Claims 1-14, 53-60 and 79-88 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not enabling all variables of R being substituted and unsubstituted. Applicants respectfully disagree.

As an initial matter, as discussed previously, only aryl, heteroaryl, aralkyl and heteroaralkyl groups can be substituted. In addition to the compounds noted by the Examiner, the present specification provides more than sufficient guidance to enable one skilled in the art to make and use compounds of Formula (I). One method for adding an R group to the piperdinyl ring is provided on page 35, lines 11-20 and shown in the scheme on page 37. Included disclosed in the present specification are the reagents and conditions for carrying out this method for adding the R group. A second method for adding an R group to the piperdinyl ring is recited on page 36, lines 1-8 and shown in the scheme on page 37. As with the first method, a list of reagents and conditions are provided in the specification. The specification also includes a third method on page 36, lines 9-24, which is shown in the scheme on page 37. Again, the specification recites reagents and conditions for this method. Additionally, as noted by the Examiner, the present specification provides a number of working examples to support enablement. Further, as acknowledged by the Examiner, the level of skill in the art is high (e.g., a masters or Ph.D. level chemists). Page 9 of the Office Action dated January 25, 2008.

Taken altogether, the present specification enables one of skill in the art to make and use the full scope of compounds encompassed by Claims 1, 8 and 14. Claims 2-7, 9-13, 53-60 and 79-88 depend directly or through one or more claims to Claims 1, 8 and 14. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph of Claims 1-14. 53-60 and 79-88

#### "Prodrugs"

Claims 1-14, 53-60 and 79-88 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly not enabling one skilled in the art to practice the full scope of the claim because the specification while enabled for "salt" is allegedly not enabled for "prodrugs". Although Applicants disagree, in order to expedite allowance of the present application the term "prodrugs" has been removed from Claims 1, 8 and 14. Claims 2-7, 9-13, 53-60 and 79-88 depend directly or through one or more claims to Claims 1, 8 and 14. Thus, Claims 1-14, 53-60 and 79-88 as amended are fully enabled by the specification as filed. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this rejection under 35 U.S.C. § 112, first paragraph.

#### Rejection of Claims 1-5, 8-12, 14, 60, 82-83 and 85-86 under 35 U.S.C. § 102(b)

Claims 1-5, 8-12, 14, 60, 82-83 and 85-86 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,216,165 (hereinafter "Mobilio"). To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379 (Fed. Cir. 1986). Moreover, pending claims must be "given their broadest interpretation consistent with the specification." M.P.E.P. § 2111, Emphasis added. Here, Applicants respectfully submit that Mobilio does not anticipate because it does not teach each and every element of the claims.

The present specification at page 11, lines 8-19, defines the term "aryl group." This definition includes a list of potential substituents for the aryl group, which includes amino and lower alkylamino. One skilled in the art understands an amino group to be -NH2 group. See Appendix A, A DICTIONARY OF CHEMISTRY 29 (3d ed. 1996). Additionally, Applicants gives two examples of amino-substituted aryl groups: 3-aminophenyl, 4-aminophenyl. See specification

page 11, lines 15-19. These examples provide support that Applicants intended an amino group to be understood as -NH<sub>2</sub>.

Moreover, Applicants have defined the term lower alkylamino. A lower alkylamino is defined in the present specification to be "lower alkyl groups connected as substituents, via a nitrogen atom, which may carry one or two lower alkyl groups." See page 10, lines 13-14. If Applicants had intended the term amino to have the broad meaning given by the Examiner it would not have been necessary to define the term alkylamino as the term amino would have encompassed all forms of substituted amine groups. In addition, as recited in the specification, lower alkyl groups are "C16 cyclic, straight-chained or branched aliphatic substituent groups connected via a carbon." Hence, lower alkyl groups do not contain heteroatoms.

Thus, the -NH-chloroisoquinoline group in Mobilio is not an amino group as that term is used in the present application because the nitrogen does not have two hydrogens attached. The -NH-chloroisoquinoline group is also not a lower alkylamino group as that term is used in the present application because the quinoline is not a lower alkyl group due to the inclusion of a nitrogen atom (i.e. a heteroatom).

Thus, in light of the specification, the -NH-chloroisoquinoline group of Mobilio is neither an amino group nor a lower alkylamino group. Therefore, Example 5, column 11 of Mobilio does not anticipate Claim 1, 8 or 14. Claims 2-5, 9-12, 60, 82-83 and 85-86 depend directly or through another claim(s) to Claims 1, 8 and 14. In view of the arguments presented above, the Examiner is respectfully requested to reconsider and withdraw this rejection.

#### Rejection of Claims 1-14, 53-60 and 79-88 under 35 U.S.C. § 103(a)

Claims 1-14, 53-60 and 79-88 stand rejected under 35 U.S.C. § 103(a) as allegedly be unpatentable over Thomas et al., *Tet. Lett.* (1997) 38:5099-5102 (hereinafter "Thomas"). To establish a prima facie case of obviousness, the claimed invention "as a whole" must have been obvious at the time the invention was made to a person of ordinary skill in the art. M.P.E.P. § 2142. To support any rejection under 35 U.S.C. § 103, there must be a clear articulation of a reason(s) why the claimed invention would have been obvious such as "[s]ome teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention,"

and a reasonable expectation of success. M.P.E.P. § 2143, (G). Applicants respectfully disagree that Thomas renders the pending claims obvious.

As acknowledged by the Examiner, the two compounds in Thomas have Ar<sub>1</sub> and Ar<sub>2</sub> being unsubstituted phenyl groups. In fact, none of the compounds in Table 3 are substituted. As stated by the Federal Circuit, "in order to find a prima facie case of unpatentability in such instances, a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention' was also required." Takeda Chemical Indus., Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1356 (Fed. Cir. 2007). The Federal Circuit further stated that "in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." Id. at 1357. Nowhere in Thomas is there disclosed a reason for modifying the compounds cited by the Examiner to include a substituted phenyl group. Thus, Thomas fails to provide the necessary reason that would have led a chemist to modify the compounds cited by the Examiner to included at least one substituted aryl ring.

Furthermore, as stated in the Manual of Patent Examining Procedure, "[i]f the prior art does not teach any specific or significant utility for the disclosed compounds, then the prior art is unlikely to render structurally similar claims prima facte obvious." M.P.E.P. § 2144.09, VI. Again, nowhere in Thomas is any specific or significant utility disclosed for the compounds cited by the Examiner.

Taken altogether, a prima facie case of obviousness has not been established. As a result, Claims 1, 8 and 14 are non-obvious over Thomas. Claims 2-14, 53-60 and 79-88 depend directly or through one or more claims to Claims 1, 8 and 14. Applicants respectfully request the Examiner reconsider and withdraw this rejection.

#### **Double Patenting**

U.S Patent No. 6,756,393

Claims 1-14, 53-60 and 79-88 have been rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-5 of U.S. Patent No.

6,756,393. Applicants respectfully request that the rejection be held in abeyance until the claims of the present application are otherwise allowable.

#### U.S Patent No. 7,253,186

Claims 1-14, 53-60 and 79-88 have been rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-21 of U.S. Patent No. 7,253,186. Applicants respectfully request that the rejection be held in abeyance until the claims of the present application are otherwise allowable.

#### U.S Patent No. 6.815.458

Claims 1-14, 53-60 and 79-88 have been rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-12 of U.S. Patent No. 6,815,458. Applicants respectfully request that the rejection be held in abeyance until the claims of the present application are otherwise allowable.

#### U.S. Patent Publication No. 2006/0194778

Claims 1-14, 53-60 and 79-88 have been provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over the pending claims of U.S. Patent Publication No. 2006/0194778. Applicants respectfully request that the rejection be held in abeyance until the claims of the present application are otherwise allowable.

#### U.S. Patent Publication No. 2006/0205722

Claims 1-14, 53-60 and 79-88 have been provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over the pending claims of U.S. Patent Publication No. 2006/0205722. Applicants respectfully request that the rejection be held in abeyance until the claims of the present application are otherwise allowable.

#### U.S. Patent Publication No. 2006/0199818

Claims 1-14, 53-60 and 79-88 have been provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over the pending claims of Application No.: 10/802,970 Filing Date:

March 16, 2004

U.S. Patent Publication No. 2006/0199818. Applicants respectfully request that the rejection be held in abevance until the claims of the present application are otherwise allowable.

U.S. Patent Publication No. 2006/0094758

Claims 1-14, 53-60 and 79-88 have been provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over the pending claims of U.S. Patent Publication No. 2006/0094758. Applicants respectfully request that the rejection be held in abeyance until the claims of the present application are otherwise allowable.

U.S. Patent Publication No. 2004/0100660

Claims 1-14, 53-60 and 79-88 have been provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over the claims of U.S. Patent Publication No. 2004/0100660. U.S. Publication No. 2004/0100660 is entitled "Image reading apparatus" with Suita-shi Tetsuya Yoshioka as the first inventor. Consequently, Applicants respectfully submit that U.S. Patent Publication No. 2004/0100660 does not present issues of double patenting for the present application.

Rejoinder

Upon allowance of the compound claims, Applicants request rejoinder or the method claims, Claims 15-49, 66-60 and 72-75, pursuant to M.P.E.P. § 821.04. Applicants also reserve the right to file continuation, divisional, or continuation-in-part applications to pursue the withdrawn subject matter.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure.

including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

#### Co-Pending Applications of Assignce

Applicants wish to draw the Examiner's attention to the following co-pending applications of the present application's assignce. Applicants respectfully request the Examiner to consider whether the claims of any one or more of the following co-pending U.S. patent applications create any issues of double patenting with respect to any of the claims of the present application; and where relevant, to consider whether the disclosure of one or more of the following co-pending applications creates any issues of patentability with respect to any of the claims of the present application. Furthermore, Applicants respectfully encourages the Examiner to monitor the prosecution of the following co-pending applications during the pendency of the present application.

Serial Number	Title	Filed
11/417790	AZACYCLIC COMPOUNDS	May 3, 2006
11/417782	AZACYCLIC COMPOUNDS	May 3, 2006
11/299566	N-SUBSTITUTED PIPERIDINE DERIVATIVES AS SEROTONIN RECEPTOR AGENTS	Dec. 12, 2005
11/417866	N-SUBSTITUTED PIPERIDINE DERIVATIVES AS SEROTONIN RECEPTOR AGENTS	May 3, 2006
11/418353	N-SUBSTITUTED PIPERIDINE DERIVATIVES AS SEROTONIN RECEPTOR AGENTS	May 3, 2006
10/759561	SELECTIVE SEROTONIN 2A/2C RECEPTOR INVERSE AGONISTS AS THERAPEUTICS FOR NEURODEGENERATIVE DISEASES	Jan. 15, 2004
11/416527	SELECTIVE SEROTONIN 2A/2C RECEPTOR INVERSE AGONISTS AS THERAPEUTICS FOR NEURODEGENERATIVE DISEASES	May 3, 2006
11/416855	SELECTIVE SEROTONIN 2A/2C RECEPTOR INVERSE AGONISTS AS THERAPEUTICS FOR NEURODEGENERATIVE DISEASES	May 3, 2006
11/416594	SELECTIVE SEROTONIN 2A/2C RECEPTOR INVERSE AGONISTS AS THERAPEUTICS FOR NEURODEGENERATIVE DISEASES	May 3, 2006

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#### Conclusion

In view of the foregoing Amendments to the Claims and Remarks, Applicants respectfully submit that this application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of this application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

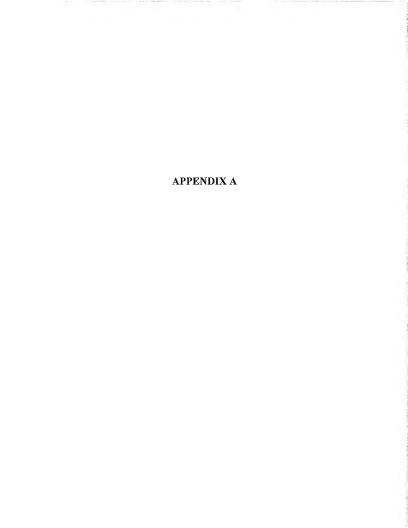
Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 4-24-08 By: Rumling

Ryan E. Melnick Registration No. 58,621 Attorney of Record Customer No. 20,995 (619) 235-8550

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### Preface

the discipant of subsequent from the contract Science Discourse, farst published by Oxford University Press in 1984 (third edition, 1986), it consists of all the entire relating to elemistry in this dictionary, notabiling physical edition, entire relating to elemistry in this dictionary, notabiling physical edition, namy new terms have been added reflecting recent advances in entire continuous contracts and managed as Testiculas crowers age is given to modern fields, such as full-trene chemistry and supramoderular chemistry.

An average bracet before a word used in an entry indicates that this word can be looked by in the deficionary and will provide further explanation of cartification. However, not every word that appears in the dictionary has an asterist's placed before it. Some entries imply feet the easter to another entry, indicating either that they are synonyms or abheviations or that they are synonyms or abheviations or othat they are most conveniently explained in one of the dictionary's longer articles. Synonyms and abheviations are usually placed within brackets immediately after the headword. Form this are explained within a neary are

displighted by being printed in take; type.

The more physical sepects of objectal chemistry and the physics itself will be found in A fortunary of Physica, which is a companion while need the dictionary. A lettinum of plants, and that is a companion when the object of clinical and objective and a fortunary of plants of the properties and the properties and to object the and the angel of the angel objects and the angel objects the angel obj

Slunits are used throughout this book and its companion volumes.

dioxide, sulphur trioxide, and aluminium oxide. Its solutions are acidic

because of hydrolysis.

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Aluminium sulphate is commercially one of the most important aluminium compounds; it is used in sewage treatment des a flocealdaring agently and in the puritacion of draibing water, the paper industry, and in the preparation of mostants; it is also a fre-proving gent, Aluminium sulphate is often wrongly called alum in these industries.

# aluminium trimethyl See trimethylaluminium.

where A is a monovalent meet the formula Agolga-Golg, 24(f., Awhere A is a monovalent meet all and B a trivalent meet. The original monovalent meet all and B a trivalent meet. The original adult is formula is of the written ARIGO-plaTHy diamninum potastism and adminitum (called present adunc is simply adult, its formula is of the written ARIGO-plaTHy diamninum meet meet a factor written ARIGO-plaTHy diamninum protastism Stocky, 27Hy (20 per potastism othoronium stuphate), etc. The allum are KCISO-plaTHy (20 per potastism othoronium stuphate), etc. The allum are superposts and or to make by disolong equivalent amounts of the two salts in water and recrystalizing, See dos alumnitum sulphate.

alunogenite A mineral form of hydrated \*aluminium sulphate, Al<sub>2</sub>(SO<sub>4</sub>), 18H<sub>2</sub>O. amalgam An alloy of mercury with one or more other metals Most metals form amalgams (from and platinum are exceptions), which may be iquid or soild. Some contain definite intermetallic compounds, such as Maffg. mention ground, An a radioactive mealitic transmirance demonstrate belonging to the "scrittorisks as 56; mass tumber of most stable isotope 2.03 (life? 26 x 19/19 sear; f.d. 1620 (1900x), m. 5.94; ±4C; hp. 260yrCope 2.03 (storoge are known. The element was discovered by G. I. Selsong and in sicropes are known. The element was discovered by G. I. Selsong and manying the element was discovered by G. I. Selsong and manying the element was discovered by G. I. Selsong and manying the element of the promised of

amethyst The purple variety of the mineral 'quartz. It is found chiefly in Brazil, the Urals Sowet Union), Arizona (USA), and Uruguay. The colour is due to impurities, especially iron oxide. It is used as a generatone.

Amide structure

amides; Organic compounds containing the group—COMBH, the amide group, Amides are Vukilte solids; examples are channed; CH5/OMH5, and proparamides (CH5/OMH5, and proparamides (CH5/OMH5, They are made by beauting the ammonium sail of the corresponding carboxylic acid, 2. Inorganic compounds containing the low INF; exp. KNH3, and CGRHFsh. Prep. are formed by the reaction of ammonia with electropositive metals.

amination A chemical reaction in which an amino group (~NH<sub>3</sub>) is introduced into a molecule. Examples of amination reaction include the reaction of halogenated hydrocarbons with ammonia (high pressure and remperature) and the reduction of nitro compounds and nitrilies.

Chy ' '' CH, primary (methylamine) tert Examples of amines

CH<sub>3</sub> CH<sub>3</sub>

aninese Organic compounds derived by replacing one or more of the hydrogen atoms in ammonia by organic groups (see Illustration). Primary mente have one hydrogen replaced, the emblyamine (LEHMS, INPA, contain the functional group -NHS, (the amito group). Scondary amines have to hydrogen replaced, the miniphyamine (LEHMS, INPA, interpretate by the decompound of the contained by the decomposition of organic matter. They can have by the decomposition of organic matter. They can be made by reducing airto compounds or amides. See also infine.

aprine safts. Safts similar to ammonium safts in which the hydrogen mount attached to the introgen are replaced by one or more organize young. Antinise resulty form safts by reaction with acids, gaining a proton to a positive resulty form safts by reaction with acids, gaining a proton soft and positive set of mannonium formyonemusis for earth pare substituted, deervatives out mannonium componemusis for earth pare substitution and an entire substitution and activities to gain and a support of the substitution of the substitution and the substitution are supported by the substitution and substitution are supported by the substitution and substitution are supported by the substitution and substitution are substitutional substitution are substitutional substitution and substitution are substitutional substitution are substitutional substitution are substitutional substitution are substitutional substitution and substitution are substitutional substitution are substitutional substitution are substitution and substitution are substitution are substitution and substitution are substitution and substitution are substitution are substitution as substitution are substitution are substitution as substitution are

When the aring has a common onsportment; name the suffix-incan be used for example, phenylamine faultine) would give [GAFAH-I/C]. known as anilinium choride Formerly, such compounds were somethnes called phenylamicate, as, aniline hydrochrofisch with the formerla Slats formed by amines are crystaline substances that are readily soluble Slats formed by amines are crystaline substances that are readily soluble.

medicinally in the form of soluble "sillodice ge, quinnea and tracipied set used medicinally in the form of soluble salts (hydrochlorides). If a last is fourth mystockies is adder to solutions of each salts the free armie is liberated. If all four hydrogen atoms of an ammonium salt are replaced by organic and the supervision is all the replaced by organic and the substantial salts are replaced by organic made by reacting textitary anises with halpogen compounds for example, the replaced by the substantial salts are substantially with chloromethate (C45,5) gives example compounds for example control and the substantial space are substantially substantially with the substantial space and the substantial space are substantially as the substantial space and the substantial space are substantially substantially substantial space are substantially substantially substantial space are substantially su

liberate the free amine when alkali is added, and quaternary hydroxides